

祛瘀消斑胶囊治疗不同类型动脉粥样硬化斑块 62 例临床研究

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摘要 目的:观察祛瘀消斑胶囊治疗不同类型动脉粥样硬化(AS)斑块的作用。方法:选择 62 例经高频超声检测确诊为周围 AS 斑块的患者,根据斑块病变类型分为脂质型、纤维脂质型、钙化型和溃疡型斑块 4 组,给予祛瘀消斑胶囊治疗,观察对斑块声学密度的影响。结果:各型斑块声学密度值均随用药时间延长而增高,变化最大的为脂质型斑块($P<0.05$),纤维型斑块次之,钙化型斑块变化率最小。结论:提示祛瘀消斑胶囊可减少脂质池和加厚纤维帽,从而稳定斑块,预防急性心脑血管临床事件的发生。

主题词 动脉粥样硬化/中医药疗法 @ 祛瘀消斑胶囊

我们用祛瘀消斑胶囊治疗不同类型的周围动脉粥样硬化(AS)患者 62 例,并利用高频超声技术观察此药对斑块声学密度的影响,现将结果报告如下。

1 临床资料

随机选择 62 例 AS 患者,男 42 例,女 20 例,年龄 36~75 岁,平均 54.5 ± 9.6 岁。临床诊断:冠心病 37 例(包括陈旧性心肌梗塞 18 例、心绞痛 19 例),原发性高血压 25 例。全部患者均经周围血管超声检查发现双侧颈动脉和股动脉中任一条动脉内膜—中层厚度(intimal—medial thickness) >1.2 mm,并经病史、查体、生化、心电图检查等,排除急性心脑血管疾病及严重肝肾疾病患者,同时参照 1994 年国家中医药管理局颁布的《中医病证诊断疗效标准》^[1],辨证属痰瘀阻络型,症见形体肥胖、胸部闷痛或刺痛、舌质紫暗、脉滑。

2 治疗及观察方法

2.1 治疗组药物:口服祛瘀消斑胶囊(药物组成为生水蛭、生山楂、大黄、海藻、莪术、地龙等,每粒胶囊含生药 0.3g,由山东大学齐鲁医院制药厂提供),每次 1.2g,每日 3 次,观察时间 8 个月,其间不服用同类或对 AS 有影响的药物。

2.2 检测方法:受试者取仰卧位,连接肢体导联心电图,行常规心电图和经胸超声心动图检查。换用高频血管探头检查双侧颈动脉和股动脉。

颈动脉超声检查:患者头部转向非检查侧,充分暴

露颈部,依次检查右侧和左侧颈动脉。首先将超声探头置于受检查者锁骨上窝处,自颈动脉起始处纵向扫查,依次显示颈总动脉、颈总动脉分叉处、颈内动脉和颈外动脉,然后将探头转动 90°,沿血管走向作短轴切面扫查,由下而上至颈内和颈外动脉,观察动脉内膜是否光滑、有无增厚、斑块部位、大小和回声特点。

股动脉超声检查:受试者下肢轻度外旋、外展,自腹股沟韧带中点起首先探查股动脉长轴切面,范围包括股动脉分叉处及分叉远端 2cm 范围内的股浅动脉和股深动脉,然后将探头转动 90°作股动脉系列短轴探查。

声学密度(AD)检测:调整仪器进入 AD—IBS 检测系统,图像采集深度 4cm, LGC 及 TGC 均调至 0 线,上述仪器条件在整个试验过程中均固定不变。仔细调整探头角度以得到理想的二维图像,在正常部位和 AS 斑块部位局部放大,进行连续 2.48s 取样。以 VHS 录像带同步记录心电图及颈动脉和股动脉超声录像,AD 检测记录于 SONY 可擦写式光盘上。

2.3 统计学处理:所有测值均以 $\bar{x} \pm s$ 表示,组间数值比较用卡方检验,治疗前后数值比较用配对 t 检验。

3 治疗结果

3.1 检测指标:脂质型斑块(I型):超声显示为较均匀的低回声内膜增厚,为脂质沉积于内膜下形成;纤维脂质斑块(IIa型)及纤维型斑块(IIb型):纤维脂质斑块的超声表现为表面有连续轮廓的回声较强的纤维帽,斑块内部脂质有明显的低回声区,如伴有斑块内出血则表现为无回声区,纤维型斑块的超声表现为局部较均匀的强回声,斑块表面有连续的回声轮廓,纤维脂质斑块和纤维型斑块为典型的动脉粥样硬化病变;钙化型斑块(III型):斑块内较多钙盐沉积,超声显示为强回声斑块,后方伴声影或较明显的回声衰减;溃疡性斑块(IV型):斑块内部出血或坏死,累及内膜面,即发生斑块破裂或内膜溃疡,致局部血小板聚集和血栓形成,超声表现为斑块表面不规则,有时呈穴状或“壁龛”样影像,溃疡边缘回声较低。声学密度分析时调整仪器设置进入 AD—IBS 状态,读取光盘信息,调整感兴趣区(ROI)的形状、方向和大小,分别置于动脉内膜和外膜,每个部位分析 62 帧图像。仪器可自动计算出内膜

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附表 AS 患者治疗前后不同类型斑块声学密度比较(%, $\bar{x} \pm s$)

斑块类型	例数	治疗前	治疗后	变化百分率
脂质型	29	61.35±5.24	68.29±4.72*	10.7%±5.91
纤维型	23	82.53±9.38	85.64±7.41	3.88%±5.64
钙化型	7	108.35±7.13	109.71±14.69	0.62%±3.71

与治疗前比较, * $P < 0.05$

(AII—I)和外膜(AII—A)的平均回声强度。为消除仪器增益、探测深度及个体差异对 AD 测值的影响,采用校正的 AII 值(AIIc%)作为统计指标, $AIIc\% = AII - I / AII - A \times 100\%$, 以此公式计算正常血管内膜和斑块的 AIIc%。

3.2 患者治疗前后各型斑块声学密度测值比较:附表表示,因溃疡型斑块例数过少,未进行统计学分析,从动脉正常内膜 AIIc%的变化分析,各型斑块声学密度值均随时间而增高,其中脂质型斑块的 AIIc%与治疗前相比有统计学差异($P < 0.05$)。

4 讨论

随着近年对斑块稳定性研究的深入,斑块的组织学特征已成为比斑块的大小更重要的反映临床预后的指标。不稳定斑块的特点是纤维帽薄,脂质池大,易于破裂,造成急性心脑血管事件。因此,AS 的消退治疗除应重视斑块体积的缩小外,更应重视斑块的质地变化,即减小脂质池,加厚纤维帽,从而稳定斑块,预防急性心脑血管临床事件的发生。

超声影像可以用不同的超声波回声强度反映斑块的组织学构成,并根据一定的标准对斑块进行组织学诊断,从而可更全面地做出临床干预的效果判断。声学密度定量技术(AD)是以背向散射积分为理论基础的定量方法^[2]。在本研究中,我们将该技术应用于斑块声学特性的定量分析。由于背向散射积分受到探头频率、探测深度、聚焦点水平等技术因素的影响,绝对测值常不能准确反映组织学的差异。动物实验的研究已经证实,内膜与外膜平均回声强度的比值(AIIc%)可排除体内检测时仪器设置、探测密度及个体差异的影响,较准确地反应内膜的声学密度。我们的研究表明,经祛瘀

消斑胶囊治疗 8 个月后,各型斑块的声学密度均有增大的趋势,说明此药能在一定程度上改变斑块的组织学构成,增大斑块的密度,起到稳定斑块的作用。祛瘀消斑胶囊组方注重活血化瘀通络,方中水蛭含有多种活性物质,其主要成分是水蛭素,它是目前最强的凝血酶抑制剂,可有效地降低血脂血小板凝聚率,改善血液的流变性,起到强有力的“破血化瘀”作用^[3];海藻咸寒,具有软坚散结、消痰化瘀之功,其提取物与水蛭相似,有抗血液凝固的作用,并能降脂降压^[4];生山楂酸甘微温,入血分,活血化瘀止痛,能通过调节脂质代谢、抗脂质过氧化、保护血管内皮细胞等途径起到延缓和抑制 AS 病变的作用^[5];莪术能抑制血小板,可通过不同途径使 TXA 的生成减少,抑制外源性 ADP 的聚集^[6];大黄苦寒,活血祛瘀,能明显降低血清胆固醇和减少肝胶原含量,防止动脉粥样硬化斑块形成^[7]。本研究显示,经本方治疗后虽然只有脂质型斑块与治疗前差异显著,但各型斑块的声学密度均有增大的趋势,说明中药复方制剂能在一定程度上改变斑块的组织学构成,增大斑块的密度,起到稳定斑块的作用,由于 AS 是一个缓慢发展的病理过程,斑块组织学构成的改变也需要很长的一段时间,若进一步延长随访时间,有可能得到更有意义的结果。

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4 体会

例 1 为小儿溃疡,临床并不少见,以十二指肠溃疡为多,临床表现常不典型,部分表现为无症状性而并发出血,该例属于此类。儿童溃疡,经胃镜检出的不少,但治疗后复查病例的报道尚少。该例用黄芪加大枣煎服,儿童的顺从性较好,对预防溃疡复发似有一定作用,值

得进一步作较多病例观察。例 2 为十二指肠巨大溃疡,十二指肠巨大溃疡是指溃疡直径在 2.0cm 以上者,其发病率为全部十二指肠溃疡的 1.6%,以男性多见。该例溃疡愈合的质量好,当于处方中的活血行瘀药促进纤维组织吸收有关。例 3 为食管溃疡,溃疡一般发生于食管中下段,该例同时还存在胃角溃疡,故仍按基本方加减,方中苏木、枳壳等有较好的促消化道动力作用。

ABSTRACTS FROM ORIGINAL ARTICLES

Clinical study on treatment of 25 cases of hepatic fibrosis after hepatitis B With Ruan Gan Mixture combined with interferon

Yan Zhongsheng, Shen Jiyun, Zhao Shuyuan

Purpose: To observe on therapeutic action of Ruan Gan Mixture combined with interferon on hepatitis B and hepatic fibrosis. **Methods:** The cases were randomly divided into the treatment group treated with Ruan Gan Mixture combined with interferon, and the control group treated with interferon, and HBV—DNA, HBeAg, hepatic function, serum HA, N—C and LN levels before and after treatment were observed. **Results:** Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), and serum HA, N—C and LN levels in the treatment group decreased significantly ($P < 0.01$), but HBV—DNA, and HBeAg negative—turning rate did not significantly change in the treatment group as compared with the control group ($P > 0.05$). **Conclusion:** Ruan Gan Mixture combined interferon have cooperative effect—increasing action in protective liver and anti—fibrosis.

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Key words: Hepatitis, B type/complication hepatic fibrosis/combined treatment of Chinese medicine and western medicine @Ruan Gan Mixture

(Original article on page 753)

Clinical study on treatment of 62 cases with atherosclerotic plaque of different types by Qu Yu Xiao Ban Capsules

Zhao Yuxia, Liu Yunfang, Zhang Mei, et al.

Purpose: To observe on the action of Qu Yu Xiao Ban Capsules on atherosclerotic plaque of different types. **Methods:** 62 cases who were diagnosed definitely to have peripheral atherosclerotic plaque were divided according to types of the plaque into 4 groups, lipoidal, fiber lipoidal, calcific type and ulcerous type plaque. They were treated with Qu Yu Xiao Ban Capsules and the effect on acoustic density of the plaque was investigated. **Results:** The acoustic density of the plaque of different types increased with prolongation of treatment time, the order of changes being lipid plaque largest ($P < 0.05$), the next fiber type, and the least calcific type. **Conclusion:** Qu Yu Xiao Ban Capsules can reduce lipid pool and thicken fibrous cap, so as to stabilize the plaque and prevent occurrence of clinical acute cardio—cerebral vascular events.

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Key words: Atherosclerosis/TCM therapy @ Qu Yu Xiao Ban Capsules

(Original article on page 755)

Clinical observation on 28 cases of uremia treated with Yi Shen Jie Du Formula combined with hemodialysis

Chen Shuanghua, Zhou Changgui, Ge Li

Purpose: To further increase the hemodialysis effect and life quality of the patient of uremia at ending stage under maintaining hemodialysis. **Methods:** Yi Shen Jie Du Formula combined with hemodialysis was used for treatment of 28 cases of uremia at ending stage, and routine hemodiagnosis was used for 28 cases as control group. They were treated for 3 months. **Results:** Time—averaged urea concentration, protein decomposition rate (PCR) and C—S indexes (KT/V) in the treatment group were significantly superior to those in the control group ($P < 0.05$). **Conclusion:** Yi Shen Jie Du Formula combined with hemodialysis is superior to the simple hemodialysis in increasing a sufficiency of hemodialysis and life quality of the patient.

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Key words: Uremia/TCM therapy @Yi Shen Jie Du Formula hemodialysis

(Original article on page 757)

Effects of Zuo Gui Pill on IL—1 and IL—6 activities in the rat of osteoporosis induced by ovariectomy

Ju Dahong, Lü Aiping, Zhang Chunying, et al.

Purpose: To explore the mechanism of Zuo Gui Pill for treatment of osteoporosis. **Methods:** In the rat of osteoporosis induced by ovariectomy, tibial bone trabecula volume percent (TBV%), tibial bone trabecula absorption percent (TRS%) and tibial bone trabecula forming surface percent (TFS%) were determined with bone tissue morphometry, and peripheral serum estradiol (E_2) content was determined by radioimmunoassay, and interleukin—1 (IL—1) and IL—6 activities were determined with mouse thymocyte detection and dependent strain cell proliferation reaction method. **Results:** Zuo Gui Pill could increase significantly TBV%, decrease TRS% and TFS%. After ovariectomy, E_2 decrease at a large amplitude greatly and IL—1 and IL—6 increased significantly, and Zuo Gui Pill did not have significant effect on E_2 content, but had a significant inhibition on IL—1 and IL—6 activities. **Conclusion:** Zuo Gui Pill can inhibit IL—1 and IL—6 activities which is one of the mechanism for prevention and treatment of osteoporosis.

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Key words: Osteoporosis/TCM therapy Zuo Gui Pill/therapeutic application

(Original article on page 777)